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A CRITICISM OF THE UNITED STATES PHARMACOPŒIA
WITH RESPECT TO THE NAMING OF THE COM-
POUND, $C_{17}H_{21}NO_4 \cdot HBr + 3H_2O$, AND WITH REGARD
TO THE PRESCRIBED TESTS FOR ITS IDENTITY AND
PURITY.

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ON THE ORIGIN AND USAGE OF THE TERMS HYOSCINE AND
SCOPOLAMINE.

The term "hyoscin" was first used by Reichardt and Höhn¹ in 1871 to designate a basic substance, $C_8H_{15}NO_2$, obtained by the action of barium hydroxide upon hyoscyamine. In 1880, Ladenburg² isolated an alkaloid from the mother-liquor obtained in the preparation of the so-called amorphous hyoscyamine from the seeds of *Hyoscyamus niger*.⁴ Ladenburg found the composition of this base to be repre-

¹ *Ann. d. Chem.* (1871), 157, p. 107.

² Later, the composition of this basic substance was found to be $C_8H_{13}NO_2$ and became known under various names, in accordance with the fancies of the respective investigators—"pseudotropin" (Ladenburg), "oxytropin" (Ladenburg and Roth), "scopolin" (E. Schmidt), and "oscin" (Hesse).

The esters of the base $C_8H_{13}NO_2$, the acetyl-, benzoyl-, and cinnamyl-esters were manufactured by the firm of E. Merck previous to the year 1898, and were sold under the name of "Scopoleins," with the name of the acid radical as a prefix, e.g., "acetyl-scopolein."—*Arch. d. Pharm.* (1898), 236, p. 33.

³ *Ber. d. deutsch. chem. Ges.* (1880), 13, p. 1549.

⁴ Bucheim was probably the first investigator to isolate the so-called "hyoscin." He obtained two basic substances from the seeds of *Hyoscyamus niger*, one of which he describes as being amorphous and oily, the other as being crystalline. To the former he gave the name "hyoscyamin" and to the latter the name "sikeranin." Cited by Ladenburg, *Ann. d. Chem.* (1881), 206, p. 283.

sented by the formula, $C_{17}H_{23}NO_3$, and thought it to be isomeric with hyoscyamine and atropine. He called it "hyoscin," as the compound obtained by Reichardt and Höhn was then thought to be identical with tropin, a decomposition product of hyoscyamine. In 1888, E. Schmidt and Henschke⁵ obtained an alkaloid from the root of *Scopolia japonica*,⁶ which, from the analysis and properties of its aurichloride, they concluded was identical with the "hyoscin" of Ladenburg. A year later, Bender⁷ isolated hyoscyamine and what he thought was a new crystalline base from the root of *Scopolia atropoides*. A quantity of this crystalline base was sent to E. Schmidt for analysis. Bender describes the properties of this alkaloid as found by Schmidt under the name "scopolin." The analysis of the product led Schmidt to review carefully his former work on the base obtained from *Scopolia japonica*, with the result that he found the composition to be $C_{17}H_{21}NO_4$ ⁸ instead of $C_{17}H_{23}NO_3$, and that it was identical with the substance received from Bender. He gave it the name "scopolamin." Furthermore, Schmidt succeeded in obtaining this base, $C_{17}H_{21}NO_4$, from several other solanaceous plants and also from commercial hyoscine hydrobromide, which was then being prepared by the firm of E. Merck. In fact, a base having the formula $C_{17}H_{23}NO_3$ and corresponding to Ladenburg's "hyoscin" could never again be isolated from the mother-liquor resulting in the crystallization of hyoscyamine, its absence being conclusively proven by L. Merck⁹ in 1897.

During the period of fifteen years following the work of Bender, the literature contains a considerable number of publications which tend to prove or disprove the identity of scopolamine and hyoscine,

⁵ *Arch. d. Pharm.* (1888), 226, p. 185.

⁶ Langaard, in 1880, reported the isolation of two alkaloids from the root of *Scopolia japonica*, which he named "scopoleine" and "rotoine" respectively.—*Pharm. Journ.* (1881), 11, p. 10.

Three years later, Eykman, working with the same root, reported the presence of but one alkaloid, to which he also gave the name "scopolein." The base isolated according to the method of Eykman was being prepared and marketed by Merck of Darmstadt and Schuchardt of Gürlitz as early as 1888. Upon analysis, Schmidt found the product to be a mixture of "hyoscin" (Ladenburg), hyoscyamine, and atropine.—*Arch. d. Pharm.* (1888), 226, p. 187.

⁷ *Chem. Zeitung* (1890), p. 805.

⁸ *Arch. d. Pharm.* (1892), 220, p. 207.

⁹ *Journ. Soc. Chem. Industr.* (1897), 16, p. 515.

some of which also tend to show the desirability of establishing the usage of the term scopolamine in preference to hyoscin, or *vice versa*. The controversy was carried on principally by O. Hesse and E. Schmidt, with an occasional opinion from others.

In 1892, when Hesse¹⁰ published his results on the identification of the Solanaceous alkaloids, he agreed with Schmidt that the composition of "hyoscin" (Ladenburg) should be represented by the formula $C_{17}H_{21}NO_4$ and that it was identical with "scopolamin," but objected to the introduction of the latter term, as the hydrobromide had already been marketed for ten years under the name of "hyoscinhydrobromid." Later, however, Hesse concluded that the two were not identical, as "hyoscin" was known to be levorotatory, and he succeeded in isolating a quantity of an optically inactive base from commercial scopolamine hydrobromide. This led him to believe that "scopolamin" was a mixture of "hyoscin" and the new base to which he gave the name "atrosin."¹¹ As early as 1890, Schmidt¹² observed that the hydrobromide was levorotatory. He also discovered that solutions of the active scopolamine hydrobromide could be rendered optically inactive by the addition of small quantities of sodium or potassium hydroxide. This change he attributed to the conversion of the optically active base into an inactive isomer,¹³ which he later isolated and called "inactive scopolamin." The identity of "atrosin" (Hesse) with the latter was conclusively proven by the work of Gadamer¹⁴ and Kuntz-Krause¹⁵ respectively.

The alkaloid represented by the formula, $C_{17}H_{21}NO_4$, was first placed upon the market in the form of the hydrobromide by Merck of Darmstadt. It was then being prepared from the base isolated from the seeds of *Hyoscyamus niger* and was sold under the name of "hyoscinhydrobromide." About 1894, shortly after the work of Bender and Schmidt, *scopolia* root became recognized as a source of supply. However, the hydrobromide, when prepared from the base obtained from the latter source, was marketed as "skopolamin-

¹⁰ *Ann. d. Chem.* (1892), 271, p. 111.

¹¹ *Ber. d. deutsch. chem. Ges.* (1896), 29, p. 1781. The term "atrosin" has never received recognition by other investigators.

¹² *Arch d. Pharm.* (1892), 230, p. 207.

¹³ *Ibid.* (1894), 232, p. 409.

¹⁴ *Ibid.* (1898), 236, p. 382.

¹⁵ *Journ. f. prakt. Chem.* (1910), 64, p. 569.

hydrobromid." Thus, E. Merck,¹⁶ in 1896, remarked that the alkaloids, hyoscyne and scopolamine, were identical, but that the name hyoscyne was given to the base when isolated from *Hyoscyamus niger*, while the term scopolamine was applied to that isolated from *scopolia* root.

In 1897, L. Merck¹⁷ called attention to some observations indicating that the hydrobromide prepared from the alkaloid obtained from *Hyoscyamus niger* was fairly constant, showing a specific rotatory power of -24° to -25° ; while that prepared in a like manner from the alkaloid when obtained from *scopolia* root varied and showed a much lower specific rotatory power, -13.47° .¹⁸ From the foregoing observations one would naturally infer that the designation hyoscyne hydrobromide would insure a product strongly levorotatory and containing little of the optically inactive isomer, while the term scopolamine hydrobromide would indicate a salt having a low specific rotatory power. Such, however, is not the case, exactly the reverse being true at the present time. The observations of Schmidt,¹⁹ Hesse,²⁰ Luboldt,²¹ and others show that the commercial salt, the hydrobromide, regardless of its natural source, often varied in its rotatory power. Schmidt attributed this variation, in the case of the salt prepared from *Hyoscyamus niger*, to the use of strong alkalies, such as the hydroxides of sodium and potassium, or even their normal carbonates on long standing, in the isolation of the free base. Furthermore, it was found that the name given to the commercial product was no indication of this variation, the salt designated hyoscyne hydrobromide varying as well as that bearing the name scopolamine hydrobromide. However, upon the introduction into the German Pharmacopœia²² of the term "Skopolamin-

¹⁶ Merck's Bericht (1894), p. 94.

¹⁷ Journ. Soc. Chem. Industr. (1897), 16, p. 515.

¹⁸ Schmidt noted a specific rotatory power of $-25^{\circ} 43'$ for scopolamine hydrobromide prepared from the base obtained from the root of *Scopolia atropoides*. He is of the opinion that the low rotatory power observed by Merck was due to the presence of i-scopolamine which may preëxist in the plant at certain seasons of the year or which may be formed in the process of curing.—Arch. d. Pharm. (1898), 236, p. 59.

¹⁹ Apoth. Ztg. (1896), 11, p. 260.

²⁰ Ibid. (1895), 10, p. 187.

²¹ Arch. d. Pharm. (1898), 236, pp. 11-47.

²² Deutsches Arzneibuch, 5th Edit., Berlin (1910), p. 451.

hydrobromid" with the specific rotatory power as a test for its identity and purity, German manufacturers began producing the lævo-salt to the exclusion of that having little or no rotatory power. Hence the name scopolamine hydrobromide, in Germany at least, now signifies the lævo-compound.

That the present tendency in England is to apply the name scopolamine hydrobromide in a manner similar to that of the German Pharmacopæia, while hyoscine hydrobromide is being used to designate the salt having the weaker rotatory power, is evidenced in the following:

(a) Spencer Sheill²³ states that scopolamine is used by some to represent the lævo-compound, while hyoscine is applied by others to the mixture of the lævo- and inactive varieties having the weaker rotatory power.

(b) A statement similar to the latter is also given in the Extra Pharmacopæia of Martindale and Westcott.²⁴

(c) Finnemore and Braithwaite²⁵ report that English physicians use the term scopolamine hydrobromide when prescribing rather than hyoscine hydrobromide in order to be sure of securing the German preparation, which is lævorotatory.

From the survey of the literature, it appears that the designation hyoscine hydrobromide is still given preference in the United States, although practically all of the salt is imported from Germany and is now being received largely as the lævo-variety.

A more concrete idea of the variations in the naming of the alkaloid and its salt, the hydrobromide, may be obtained from the following tabulations:

TABLE NO. 1.

NAMES APPLIED TO THE FREE BASE OR RELATED COMPOUNDS.

Atroscin....	Hesse, 1896 = $C_{17}H_{21}NO_4$, isolated from commercial scopolamine hydrobromide, optically inactive and identical with i-scopolamine.
	Reichardt and Höhn, 1871 = $C_8H_{16}NO$, a decomposition product of hyoscyamine.
Hyoscin....	Ladenburg, 1880 = $C_{17}H_{23}NO_3$, isolated from <i>Hyoscyamus niger</i> .
	Schmidt and Henschke, 1888 = a base isolated from <i>Scopolia japonica</i> .
	Hesse, 1892 = $C_{17}H_{21}NO_4$, isolated from <i>Hyoscyamus niger</i> .
	E. Merck, 1894 = $C_{17}H_{21}NO_4$, isolated from <i>Hyoscyamus niger</i> .

²³ *Lancet* (1910), II, p. 29.

²⁴ Martindale and Westcott, Extra Pharmacopæia, London (1912), p. 444.

²⁵ Year-Book of Pharm. and Trans. (1912), p. 498.

Scopolamin.	Schmidt, 1890 = $C_{17}H_{21}NO_4$, isolated from <i>Scopolia japonica</i> .
	Schütte, 1891 = $C_{17}H_{21}NO_4$, isolated from <i>Datura stramonium</i> .
	Schmidt, 1892 = $C_{17}H_{21}NO_4$, isolated from <i>Datura stramonium</i> , <i>Duboisia myoporoides</i> , and <i>Atropa belladonna</i> .
	E. Merck, 1894 = $C_{17}H_{21}NO_4$, isolated from <i>Scopolia</i> root.
Inactive Scopolamin.	Thoms and Wentzel, 1898 = $C_{17}H_{21}NO_4$, isolated from <i>Mandragora</i> root.
Scopoleine.	Schmidt, 1896 = $C_{17}H_{21}NO_4$, the optically inactive isomer.
Scopoleins.	Langaard, 1881 = a mixture of alkaloids from <i>Scopolia japonica</i> , principally $C_{17}H_{21}NO_4$.
Scopolin.	Firm of Merck, 1898 = esters of the base, $C_8H_{13}NO_2$.
	Bender, 1890 = $C_{17}H_{21}NO_4$, isolated from <i>Scopolia japonica</i> .

TABLE NO. 2.

OFFICIAL NAMES AND SYNONYMS OF THE HYDROBROMIDE.

Hyoscinæ hydrobromicum.....	} British Pharmacopœia, 1898.
Hyoscine hydrobromide.....	
Hydrobromate of hyoscine.....	
Scopolamine hydrobromide.....	
Hyoscinæ hydrobromidum.....	} United States Pharmacopœia, 1905.
Hyoscine hydrobromide.....	
Hyoscinæ hydrobromas, 1890.....	
Scopolaminæ hydrobromidum.....	
Scopolamine hydrobromide.....	} French Pharmacopœia, 1908.
Neither the free base nor its salt, the hydrobromide, is official.....	
Bromidato di Scopolamina.....	
Scopolaminum hydrobromicum.....	
Scopolaminhydrobromid.....	} Italian Pharmacopœia, 1909.
	} German Pharmacopœia, 1910.

ON THE PHYSIOLOGICAL ACTION OF SCOPOLAMINE.

Scopolamine is an ester of tropic acid and the base, scopolin,²⁶ and, like the closely related hyoscyamine, may exist in three stereoisomeric forms. Two of these, the levo- and racemic forms, are known. These isomers, like those of nicotine²⁷ and hyoscyamine,²⁸ differ in their physiological action as well as in their chemical and physical properties.

The early investigators who attempted to discover a difference in the physiological action of the two isomers did not work with the material prepared in their own laboratories, and very probably used the salts in an impure state; *i.e.*, as mixtures of the two isomers or with small amounts of other impurities²⁹ present. Add to this

²⁶ Gadamer, *Arch. d. Pharm.* (1901), 239, p. 321.

²⁷ *Ber. d. deutsch. chem. Ges.* (1904), 37, p. 1234.

²⁸ Cushny, *Journ. of Physiol.* (1904), 30, p. 176.

²⁹ Schmidt, Scopolamine hydrobromide with a low specific rotatory power contains a small amount of an impurity not easily detected.—*Arch. d. Pharm.* (1905), 243, p. 4.

the lack of chemical knowledge concerning the substance with which they were working and we can readily understand why they obtained varying and sometimes contradictory results.

Königshoefer³⁰ reported that the effect of atropine (i-scopolamine) upon the accommodation takes place with greater rapidity and is of longer duration than in the case of scopolamine (l-scopolamine). Under pathological conditions (iritis) he also found its action to be the more energetic.

Meyer confirmed³¹ the latter finding, but stated that he could not agree with Königshoefer with respect to the action on the accommodation.

Uthoff and Axenfeld³² could find no difference in the physiological action of scopolamine hydrobromide having a specific rotatory power of -25.43° and that having specific rotatory power of -6.62° .

In more recent years the work has been taken up with a greater knowledge of the chemistry of the isomers and under more advantageous conditions, with the result that real differences in their physiological activity have been found and clearly described.

Cushny and Peebles³³ found:

(a) That the action of l-scopolamine on the terminations of the secretory nerves in the salivary glands and on the terminations of the inhibitory fibres of the heart was double that of i-scopolamine in effect; from which they inferred that a similar ratio might hold in other analogous terminations.

(b) That l- and i-scopolamine produce the same effect in a like degree upon the central nervous system in man and mammals and on the terminations of the motor nerves in the frog.

E. Hug,³⁴ from a series of experiments on dogs and cats, concluded:

(a) That the action of l-scopolamine on the vagus is three to four times as great in strength as that of i-scopolamine.

(b) That l-scopolamine acts twice as energetically as i-scopolamine upon the oculomotorius.

Evidence to the effect that a difference in the physiological action

³⁰ Cited by Hesse, *Ber. d. deutsch. chem. Ges.* (1896), 27, p. 1781.

³¹ Cited by E. Schmidt, *Arch. d. Phar.* (1897), 236, p. 71.

³² Cited by L. Merck, *Pharm. Journ.* (1897), 71, p. 41.

³³ *Journ. of Physiol.* (1905), 32, pp. 501-510.

³⁴ *Arch. f. exp. Path. u. Pharmac.* (1912), 69, p. 56.

of the commercial preparations has been observed by medical practitioners is amply supplied in the literature. In fact, the references are too numerous to be included in this paper. However, the statement of Finnemore and Braithwaite³⁵ in connection with the use of hyoscine and scopolamine hydrobromides by English physicians is quoted because of the direct application:

"Anæsthetists have expressed a preference for the German preparations sold under the name of 'Scopolamine hydrobromide' owing to the variable results obtained following the administration of the product known as 'Hyoscine hydrobromide.'"

ON THE TESTS FOR IDENTITY AND PURITY.

The chemical and physical properties of scopolamine and its salts have been quite thoroughly worked up by E. Schmidt, O. Hesse, Gadamer, and others. There is, however, some uncertainty concerning the melting-points of the chloraurates of both the l- and i-scopolamine, the greater number of the investigators confirming the results obtained by Schmidt. The following tables show the important physical constants of the hydrobromides as obtained by various investigators and as given in the United States, British, and German Pharmacopœias:

TABLE NO. 3.

Name of investigator.	Stereoisomer.	M. P. of the anhydrous salt.	M. P. of the chloraurate.	M. P. of the hydrobrom-chloraurate.	M. P. of the picrate.	Specific rotatory power in aqueous solution.
E. Schmidt ³⁶	Lævo-	193-194°	212-214°	187-188°	-25° 43'
E. Schmidt.....	Inactive	180°	208-210°	0°
Gadamer ³⁷	Inactive	208°	0°
Kircher ³⁸	Lævo-	208-209°	-25° 52'
Thoms and Wentzel ³⁹	205°
O. Hesse ⁴⁰	Lævo-	192-197°	198°	-25.7° to -25.0°
O. Hesse.....	Inactive	181°	201-202°	0°
Jowett ⁴¹	Lævo-	About 215

³⁵ Year-Book of Pharm. and Trans. (1912), p. 498.

³⁶ *Arch. d. Pharm.* (1898), 236, p. 59.

³⁷ *Ann. d. Chem.* (1900), 310, p. 352.

³⁸ *Arch. d. Phar.* (1905), 243, p. 321.

³⁹ *Ber. d. deutsch. chem. Ges.* (1898), 31, p. 2037.

⁴⁰ *Journ. f. prakt. Chem.* (1901), 64, 2, p. 364.

⁴¹ *Journ. Chem. Soc.* (1897), 71, p. 678.

In explanation of the table it should be stated that Schmidt and Gadamer determined the melting-points of the various salts, using a capillary tube and sulphuric acid bath; Hesse used a "Roth's" apparatus. Schmidt found the melting-point of the chloraurate of the l- salt to be 208° to 209° when determined with the "Roth's" apparatus.⁴²

TABLE NO. 4.

Pharmacopœia.	Per cent. of H ₂ O lost in drying at 100° C. or over H ₂ SO ₄	M. P. of the anhydrous salt.	M. P. of the chloraurate.	Specific rotatory power of a 5 per cent. aqueous solution at 15° C.
United States ⁴³	179.7°	197°
British ⁴⁴	More than 12 per cent.	193-194°	198°
German ⁴⁵	12.3 per cent.	About 190°	-24° 45'

A comparison of the constants as given in Tables No. 3 and No. 4 shows the melting-point (179.7° C.) of the anhydrous hydrobromide as specified in the United States Pharmacopœia to agree very closely with that (180° C.) found by Schmidt or Hesse (181° C.) for i-scopolamine hydrobromide; while the melting-point (197° C.) of the chloraurate as given in the pharmacopœia corresponds very well with that (198° C.) found by Hesse for the chloraurate of l-scopolamine. According to two observers, the melting-point of the hydrobromide alone is no indication as to the respective quantities of the l- and i-isomers present in the commercial salt; *e.g.*, Schmidt⁴⁶ found a melting-point of 180°-181° C. for the commercial hydrobromide, $[\alpha]_D = -13^\circ 30'$; Hesse⁴⁷ obtained a melting-point of 178° C. for a sample of the hydrobromide, $[\alpha]_D = -21.3^\circ$. If we take into consideration the fact that the hydrobromides of both the lævo- and the inactive forms crystallize with 3H₂O, and that the melting-points of the chloraurates have not yet been definitely established, it becomes evident that the pharmacopœial tests for the identity of this compound are worthless.

That physical constant which has been found to give the most accurate indication as to the purity of l-scopolamine or its salts,

⁴² *Arch. d. Phar.* (1894), 232, p. 417.

⁴³ U. S. P., 8th Rev. (1905), p. 391.

⁴⁴ *British P.* (1898), p. 153.

⁴⁵ *Deutsches Arzneibuch*, 5th Edit., Berlin (1910), p. 451.

⁴⁶ *Arch. d. Pharm.* (1898), 236, p. 62.

⁴⁷ *Journ. f. prakt. Chem.* (1901), 64, 2, p. 385.

both with respect to the presence of the inactive variety and to foreign substances, is the specific rotatory power. This has been found to be between -24° and -25° for the fairly pure anhydrous hydrobromide in a 5 per cent. aqueous solution at 15° C. A specific rotatory power of -32.3° to -32.9° has been found by Hesse⁴⁸ for the salt in a high state of purity. Determinations of this constant have revealed the following variations in the commercial product:

1894—E. Schmidt⁴⁹: Scopolamine hydrobromide from Gehe and Company, Dresden. $[\alpha]_D = -14.58^{\circ}$.

1895—E. Schmidt⁵⁰: Scopolamine hydrobromide from E. Merck, Darmstadt. $[\alpha]_D = -17^{\circ} 9'$.

1895—Gadamer⁵¹: Scopolamine hydrobromide from Gehe and Company, Dresden. Anhydrous salt in aqueous solution, $p = 6.3043$, $t = 19.8^{\circ}$ C., $[\alpha]_D = -6.62^{\circ}$.

1896—O. Hesse⁵²: Five commercial samples of scopolamine hydrobromide showed a specific rotatory power as follows: -22.1° , -12.7° , -12.1° , -11.3° , -10.0° .

1897—L. Merck⁵³: Scopolamine hydrobromide from *Scopolia* root, $[\alpha]_D = -13.47^{\circ}$. Scopolamine hydrobromide from the seed of *Hyoscyamus niger*, $[\alpha]_D = -24^{\circ}$ to -25° .

1898—Luboldt⁵⁴: Scopolamine hydrobromide from Gehe and Company, Dresden. 1.5304 Gm. of anhydrous salt in aqueous solution, $d = 1.0096$, $t = 15^{\circ}$, $[\alpha]_D = 14^{\circ} 58'$.

1899—O. Hesse⁵⁵: Scopolamine hydrobromide, commercial. Anhydrous salt in aqueous solution, $p = 4$, $t = 15^{\circ}$, $[\alpha]_D = -7.5^{\circ}$.

1901—Gadamer⁵⁶: Scopolamine hydromide from E. Merck, Darmstadt. $[\alpha]_D = -24.69^{\circ}$.

1912—E. Hug⁵⁷: Scopolamine hydrobromide from Hoffmann-La Roche Company, Grenzach. Anhydrous salt in aqueous solution, $p = 4.5$, $[\alpha]_D = -26.0^{\circ}$.

1912—Finnemore and Braithwaite⁵⁸: Four samples of commercial hyoscine hydrobromide showed a specific rotatory power as follows: $-23^{\circ} 7'$, $-21^{\circ} 59'$, $-21^{\circ} 25'$, $-6^{\circ} 30'$; one sample was found to be inactive.

⁴⁸ Journ. f. prakt. Chem. (1901), 64, 2, p. 385.

⁴⁹ Apoth. Ztg. (1896), 11, p. 260.

⁵⁰ Ibid.

⁵¹ Cited by Schmidt, Arch. d. Pharm. (1898), 236, p. 47.

⁵² Ber. d. deutsch. chem. Ges. (1896), 29, p. 1780.

⁵³ Journ. Soc. Chem. Industr. (1897), 16, p. 575.

⁵⁴ Arch. d. Phar. (1898), 236, p. 14.

⁵⁵ Ann. d. Chem. (1899), 309, p. 90.

⁵⁶ Arch. d. Phar. (1901), 239, p. 324.

⁵⁷ Arch. f. exp. Path. u. Pharmak. (1912), 69, p. 48.

⁵⁸ Phar. Journ. and Trans. (1912), p. 498.

CONCLUSIONS AND SUGGESTIONS.

1. Practically all of the scopolamine hydrobromide or the so-called hyoscine hydrobromide consumed in the United States is at present supplied by Germany, where the lævo-compound only is recognized as official under the title "Skopolaminhydrobromid." In view of this fact, and as present usage, not only in Germany but in other continental countries and in England, indicates a preference for the latter term, there can be no important reason for the same compound appearing under two different titles in the United States Pharmacopœia. It is therefore suggested that the term "Scopolamine hydrobromide" be made the official English title in the next revised edition of the pharmacopœia, with "Hyoscine hydrobromide" as a possible synonym.

2. As there is still some doubt concerning the exact melting-point of the chloraurate of either the l- or i-scopolamine, this constant should not be prescribed as a test by the next pharmacopœia.

3. It is now known that scopolamine or the so-called hyoscine may exist in either the lævo- or inactive forms, and that the commercial hydrobromide is usually the lævo-salt, but not infrequently a mixture of the two isomeric forms. It is also known that the isomers produce different physiological effects, the lævo- variety preferred by medical practitioners because of its particular physiological action and on account of its constant state of purity. It is therefore suggested that the revised edition of the United States Pharmacopœia recognize only the l-scopolamine hydrobromide as official, and that a definite specific rotatory power be prescribed for it.

CONSTITUENTS OF ANDROGRAPHIS PANICULATA.

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Andrographis paniculata, Nees (Fam. *Acanthaceæ*), is a common bitter plant growing throughout the plains of India. The plant is an annual one, two to three feet long; stem quadrangular, pointed, smooth; leaves opposite, on short petioles, lanceolate, entire upper surface dark green and shining, under surface paler and finely granular; they vary much in size, but the larger are usually three inches in length and one inch in breadth; calyx deeply five-cleft, corolla bilabiate, tips linear, reflected, upper one three-toothed, lower

one two-toothed; flowers remote, alternate, long petioles, downy, rose colored or white streaked with purple; capsules erect, somewhat cylindrical; seeds, three to four in each; roots fusiform, simple woody with numerous fine radicles.

The plant is well known in Bengal under the name of Kalmegh, and is the principal constituent of a domestic medicine named Alui which is given to children for the relief of griping, irregularity of bowels, and loss of appetite. It is also called Kiryat, and is used as a substitute for chirata. It is called in Sanskrit "Mahatikta," or king of bitters.

According to Dr. W. A. Boorsma (Mededeelingen uit S Lands plantentium, 1896, xviii, 63), if the powdered plant be mixed with lime and submitted to steam distillation, the distillate gives all the tests of a volatile alkaloid which he could not isolate. He, however, isolated an amorphous bitter substance ($C_{15}H_{27}O_4$).

He says that the substance begins to decompose before melting, so that he could not determine its melting-point accurately. The amorphous substance obtained by the present author has some properties common with the above substance, but the melting-point has been accurately determined; while the above author says that the amorphous and crystalline (also obtained by him) substances have the same properties, the two substances described herein have very different properties.

Dr. K. Gorter, by extracting the leaves of *Andrographis paniculata* with alcohol, obtained a lactone ($C_{22}H_{30}O_5$) named andrographolite. It is converted into salts of andrographic acid by boiling with caustic alkalies (*Apoth. Zeits.*, 1911, 26, 954).

EXPERIMENTAL.

For examination 68 Gm. of the powdered leaves and stems were taken and exhausted in a Soxhlet apparatus successively by petroleum ether, ether, chloroform, and alcohol; after evaporation of the solvents the extracts weighed:

Petroleum ether	0.437 Gm., or 0.643 per cent.
Ether	0.5864 Gm., or 0.861 per cent.
Chloroform	2.2501 Gm., or 3.309 per cent.
Alcohol	1.5045 Gm., or 2.214 per cent.
Total	7.027 per cent.

55 Gm. of substance on burning gave 9.7802 Gm. or 17.782 per cent. of ash.

The plant is very rich in chlorophyll, one portion of which is soluble in chloroform and the other not, though both are soluble in alcohol.

EXAMINATION OF THE PETROLEUM ETHER EXTRACT.

This was a viscid, brownish-yellow colored liquid from which, on keeping a small quantity of an inactive, needle-shaped crystalline substance separated out, having 117° C. as its melting-point, the quantity obtained was so small that no further examination was possible. The viscid mass also contained a little essential oil, which was separated by extraction with alkalis; the rest of it was "kalmegh resin," a portion of which was extracted by first making it alkaline with caustic potash and shaking up with ether. It can be further extracted with ether after acidification with an acid.

CHLOROFORM EXTRACT.

This contained besides chlorophyll an amorphous white substance and very little of a bitter substance, the former of which separated out on concentrating the chloroform extract. Its melting-point is 221° C. It is tasteless and insoluble in water and alcohol. It is unacted upon by acids and alkalis.

EXTRACTION OF THE BITTER PRINCIPLES.

For this extraction the powdered leaves and stems were exhausted in a percolator with alcohol, almost the whole of which was distilled off. The thick, viscid mass left in the flask was then submitted to steam distillation. Two or three drops of an essential oil first came over; this had an intensely characteristic odor suggesting that of the dried plant. The distillation continued till the whole of the alcohol was distilled off. The residue remaining in the flask separated into two layers, one aqueous and the other solid; the former when allowed to cool deposited some yellow colored crystals (bitter *a*); the latter was boiled with water and filtered hot; from the filtrate a white amorphous precipitate was deposited having an extremely bitter taste (bitter *b*).

EXAMINATION OF THE BITTER PRINCIPLE (A).

This was purified by dissolution in alcohol and fractional precipitation; the process was repeated three times. It had a pale yellow color. When a little of the substance was heated in a test-tube it diffused a very fragrant odor. It had melting-point of 206° C.

Strong sulphuric acid produced a yellowish-brown color. With potassium dichromate and sulphuric acid the substance at first gave a deep brown (almost black) color, attended with brisk effervescence. After a time the effervescence ceased and the color passed to grass-green.

Strong sulphuric acid containing a trace of nitric acid produced a reddish-brown color.

Strong sulphuric acid containing ammonium vanadate produced brownish-red color, changing to green.

In strong nitric acid the substance dissolved readily, the solution acquiring a yellow color.

The substance is very soluble in ethyl and methyl alcohol, though not to the above extent in amyl alcohol. It is very slightly soluble in chloroform and ether. Benzene and petroleum ether do not dissolve it even on boiling.

It is neither an alkaloid nor a glucoside, as it neither contains nitrogen nor produces a reducing sugar after hydrolysis. It can be acetylated,—i.e., it contains hydroxyl groups; the acetyl derivative is white and insoluble in water. Its melting-point is 95° C.

When the substance was added to a solution of bromine in chloroform a dark-colored oil separated out; on washing the latter with a dilute solution of potassium carbonate a white solid substance was left behind. This was the bromo derivative of the bitter; the direct absorption of bromine proves the presence of at least one double bond. The melting-point of the bromo derivatives would not be determined, as it began to decompose at 120° C. before melting; at 160° C. it was a liquid, but began to give off a quantity of gas.

0.0498 Gm. of the bromo derivative gave 0.0160 Gm. of AgBr or 13.7 per cent. of bromine. Since there must be at least two atoms of bromine in the molecule, the molecular weight is 1175 or some multiple of it.

0.1008 Gm. of the bitter analysis gave 0.2521 Gm. of CO_2 and 0.0763 Gm. of H_2O .

Hence C 68.2, H 8.4.

The simplest formula is $C_{10}H_{28}O_5$.

The molecular weight of the bitter principle as determined from the bromo-compounds is 1015, which is exactly six times that of the empirical formula.

The acetyl derivative gave the following analytical data:

It contains 1.74 per cent. of water.

0.0697 Gm. of it gave 0.1863 Gm. of CO_2 and 0.05056 Gm. of H_2O .

Hence C 76.2 H 8.06.

EXAMINATION OF THE BITTER PRINCIPLE (B).

It was a white amorphous substance having an extremely bitter taste. It is odorless, and its melting-point is $185^\circ C$. It is practically insoluble in cold water. When a little of the substance was boiled for a long time with water the latter acquired a slightly acid reaction. It is soluble in alcohol and chloroform. In the Pharmacographia of Fluckiger and Hanbury it is said that an infusion gives a voluminous precipitate with tannic acid, but this property was altogether found to be absent. Most probably in the former case the precipitate was due to the presence of some albuminous matter. Sulphuric acid produces an orangish-yellow color; when potassium dichromate is added to the above the color changes as one to yellow-green, which through greenish-brown finally passes to deep grass-green. If the substance be mixed with potassium dichromate before the addition of sulphuric acid, and the acid then added, the color first produced is brown, but the final color in this case also is deep grass-green.

Strong sulphuric acid containing a trace of nitric acid gives a brown color.

Strong sulphuric acid containing a trace of ammonium vanadate produces a brown color, changing to violet.

Strong nitric acid does not produce any change.

0.409 Gm. gave 0.0448 Gm. of H_2O and 0.0930 Gm. of CO_2 .
C 62.01, H 14.88 and O 23.01.

The formula $C_{19}H_{51}O_5$ is given to it, for which the theoretical values are—

C 62.24, H 14.7 O 23.01.

The name Kalmeghin is proposed for it.

A white substance separated out when bitter (b) was treated with an acid.

This was washed with water and dried. It had an acid reaction and was soluble in alkalis, neutralizing it. As it was derived from Kalmeghin the name Kalmeghic acid was given to it.

0.043 Gm. gave 0.0699 Gm. of H_2O and 0.2053 Gm. of CO_2 .

Hence C 75.23 H 10.4.

The formula is $C_{14}H_{23}O_2$.

This acid, as well as the bitter principle (b), gave fluorescein test, showing the presence of a benzene nucleus with two adjacent side chains.

CHEMICAL LABORATORY, PRESIDENCY COLLEGE, BENGAL.

ON THE DETERMINATION OF ACETANILID.

By DR. A. MIRKIN, Cincinnati, Ohio.

The determination of acetanilid in tablets is still effected by an extraction with chloroform, the chloroform being collected in a tared flask, evaporated, and the residue dried at a low temperature and weighed. This method frequently gives low results on account of the volatility of acetanilid, and very often it is not applicable at all on account of the presence of other ingredients in the tablets which are also soluble in chloroform.

The volumetric method adopted by the Association of Official Agricultural Chemists, in which a solution of potassium bromide-bromate is used, does not always give accurate results, and it seemed desirable to find another method which might prove successful when other methods failed.

Bay and Vignon (*Comptes Rend.*, 135, 507; *Centralblatt*, 1902, ii, 1094) determine nitrous acid by titrating with a standard solution of aniline. The nitrous acid is used up in diazotizing the aniline. As soon as the nitrous acid is gone a piece of potassium iodide-starch paper, with which the solution is tested from time to time, does not turn blue any more. This reaction is reversible, and one can titrate aniline with a standardized solution of sodium nitrite. By converting acetanilid into aniline and titrating with a standard sodium nitrite solution, we have a quick method of determination. In order to obtain correct results all the conditions mentioned below must be strictly adhered to.

One gramme of acetanilid is boiled for four hours with a mixture of one part sulphuric acid (sp. gr. 1.84) and five parts water. The solution is then cooled and carefully neutralized with sodium bicarbonate. HCl is then added (6 mol. to 1 mol. anilin) and the flask is cooled to -10° by throwing in pieces of ice and using a freezing mixture. The sodium nitrite is then slowly added from a burette with thorough shaking of the flask after each addition. From time to time the solution is tested with potassium iodide-starch paper. It frequently happens that the potassium iodide-starch paper turns blue even when there is unchanged aniline. This is due to the low temperature, which causes the diazotizing to take place slowly. One must therefore not be too hasty in his conclusions, especially at the end, but wait several minutes after the addition of sodium nitrite before applying the KI-starch paper test.

As mentioned above, Bay and Vignon, the originators of this method, should be given full credit. I have only adapted their method of determining aniline to the determination of acetanilid.

PREPARATION AND ANALYSES OF VLEMINCKX'S SOLUTION.¹

By JOSEPH L. MAYER.

A short time ago two samples of Vleminckx's Solution were submitted to me with a request that in view of the fact that the color of one sample was markedly different from the other, analyses be made to ascertain if they were properly prepared.

Since the National Formulary only contains a formula for the preparation, and various pharmaceutical authorities consulted made no reference to a standard, it was necessary to make samples in an effort to determine how the solution should be prepared and what the strength of the finished product should be. The following work was therefore undertaken.

Referring to page 81, 3rd edition of the National Formulary, we found that "Liquor Calcis Sulphuratæ"—"Vleminckx's Solution"—was directed to be prepared as follows:

Lime, freshly slaked165 grammes.
Sublimed sulphur250 grammes.
Water, a sufficient quantity to make 1000 grammes.

¹ Read before the Kings County Pharmaceutical Society, May 12, 1914.

Mix the slaked lime with the sulphur, and add the mixture gradually to 1750 c.c. of boiling water. Then boil the whole, under constant stirring, until it is reduced to 1000 grammes, strain, and having allowed the solution to become clear by standing in a well-stoppered bottle, decant the clear brown liquid, and keep it in completely filled and well-stoppered bottles.

We accordingly made up one-tenth of this formula by taring a 600 c.c. porcelain evaporating dish, adding 175 c.c. of water heating to boiling and then slowly adding the mixture of freshly slaked lime and sulphur, constantly stirring while heating until the weight was reduced to 100 grammes. The material was then decanted into a 4 oz. cork stoppered bottle, allowed to stand until the next day, filtered and assayed for total sulphur by the following method:

"Measure 10 c.c. of the clear sample in a 100 c.c. measuring flask and fill to the mark. Analyze 10 c.c. aliquots of this solution. Treat with 3 c.c. of saturated solution potassium hydroxide or sodium hydroxide solution, following by 50 c.c. hydrogen peroxide free from sulphates. Heat on the steam bath for one-half hour exactly and then acidify with hydrochloric acid, precipitate with barium chloride in the usual way in boiling solution, and finally weigh as barium sulphate." Of course multiplying the weight of barium sulphate by the proper factor gives the quantity of sulphur and this multiplied by 100 gives the percentage.

We ran blanks on the reagents and determined the quantity of sulphate present, which was then deducted from that found in the actual analysis.

This is Avery's method, and is suggested by the Association of Official Agricultural Chemists for the analysis of lime-sulphur dips and lime-sulphur-salt mixture (U. S. Dept. Agr. Bureau of Chemistry, Bul. 107, rev. page 34); it is an extremely accurate and simple one which in our hands yielded remarkably close duplicates.

We also analyzed the sample for total sulphur in solution, monosulphur equivalent, thiosulphate sulphur, sulphate and sulphite sulphur, total sulphide sulphur and total lime (CaO) in solution following the method in U. S. Dept. Agr. Bureau of Chemistry, Bul. 162, page 29, but seeing no advantage over the Avery method, employed that in all our analyses and simply determined the total sulphur, of which the above sample showed the presence of 10.838 grammes in 100 c.c. of solution.

Another 100 gramme lot made up in the same manner contained 14.581 grammes of total sulphur in 100 c.c. of solution.

This great variation in results indicated difficulty in properly preparing the solution. We, therefore, referred to the direction in the N. F. and found it directed to add the lime and sulphur mixture "gradually to 1750 c.c. of boiling water. Then boil the whole under constant stirring until it is reduced to 1000 grammes;" this procedure differs from mine in that it directs the water to be heated to boiling, the mixture of lime and sulphur added and the whole boiled under constant stirring until the weight is reduced to 1000 grammes.

Another 100 gramme lot was then made by strictly adhering to these directions and when assayed showed the presence of 4.448 grammes of total sulphur in 100 c.c. solution.

My original reading of the process was as above noted to heat the water to boiling and then while the water was still on the fire to gradually add the lime and sulphur under constant stirring and boiling until the proper weight was produced, whereas the last product was made by strictly following the N. F. by heating the water to boiling, taking it off the fire, stirring all the lime and sulphur in, putting it back on fire, stirring and heating until the proper weight was attained.

The above figures clearly indicated that the wording of the manipulation in the N. F. was faulty, therefore another batch of 100 grammes, employing the official quantities, was made by taring a 250 c.c. Erlenmeyer flask, adding 175 c.c. of water heating on the hot plate until boiling and then adding the lime and sulphur previously mixed and boiling on the hot plate without stirring or further attention until the weight was reduced to 100 grammes, transferred to a 4 oz. cork stoppered bottle, allowed to stand until the next day, filtered and assayed.

The solution contained 29.162 grammes of total sulphur in 100 c.c.

Another lot made by the same method contained 29.593 grammes of total sulphur in 100 c.c. solution.

These figures indicate that if the solution is prepared in a flask the product will practically be of uniform strength.

It is true the N. F. does not state whether a flask or evaporating dish should be employed. The result of the failure to specifically state that a flask or similar vessel be used is shown by the analyses

to yield preparations of indefinite strength. If a large enough flask is not at hand, vessels which are deep should be employed, the object being to avoid too rapid evaporation of water, as the proper preparation of the product requires several hours.

In view of the above results the Committee on National Formulary should revise the wording of the directions for the preparation of Vleminckx's solution, and thus insure a uniform product. Of course if thought necessary a standard could be fixed for the preparation and a method of assay appended.

I would take this opportunity to acknowledge my indebtedness to my assistant, J. H. Wiener, Ph.C., for assistance rendered in the preparation and analyses of some of the samples.

A NOTE ON THE VALUE OF PRESERVATIVES IN SYRUP OF IRON IODIDE.¹

By GEORGE M. BERINGER.

In the U. S. P. 8th Revision, diluted hypophosphorous acid to the extent of 20 Cc. to 1000 Gm. has been added to this syrup as a preservative. Several of the foreign pharmacopœias have used organic acids for the same purpose, the Austrian Pharmacopœia directing 0.1 per cent. of citric acid, the Swiss Pharmacopœia 0.05 per cent. of citric acid, and the French Pharmacopœia 0.1 per cent. tartaric acid. The German Pharmacopœia, the British Pharmacopœia, the Danish Pharmacopœia, the Swedish Pharmacopœia, and the Italian Pharmacopœia do not direct any preservative, dependence being placed upon the use of sufficient sugar.

In order to test out the relative value of these preservatives, six samples of syrup of iron iodide were prepared on October 15, 1913. In all of these the official process and manipulation and percentage of iron salt and sugar were carefully followed. These samples were preserved in my laboratory and not exposed to direct sunlight for several months. On December 18th, their condition was observed and noted. Subsequently these samples were filed with Chairman Remington and preserved in his laboratory with the other pharmacopœial samples until a few days ago, when I obtained them for observation of the further changes that had

¹ Read at the meeting of the New Jersey Pharmaceutical Association, Lake Hopatcong, June 17, 1914.

taken place. In the tabulation below the appearance on these two dates of each sample is noted:

No. 1.—Proportions of the U. S. P. formula, but without any preservative. On December 18th this sample was slightly yellow. It is now of a pale green color and appears to be in perfect condition.

No. 2.—U. S. P. 8th formula without any variation. On December 18th this sample was very pale but perfectly clear. It was noted that the green color had gradually faded out and the sample was much lighter in color than when first prepared. This is in accordance with the observations on this formula that had been previously reported.

This sample is now of a light yellow color and there is evidence of some change in the sugar, the change that we have commonly considered as caramelizing which takes place in the presence of hypophosphorous acid to a moderate extent.

No. 3.—Proportions of the U. S. P. with the addition of 0.05 per cent. of tartaric acid. This sample, on December 18th, had assumed a distinct yellow color. It has now faded until it is almost colorless.

No. 4.—Proportions of the U. S. P. formula with 0.1 per cent. of tartaric acid. On December 18th this sample had retained the light green color about the same tint as when first prepared. It now shows no change and appears to be in perfect condition.

No. 5.—Proportions of the U. S. P. formula with the addition of 0.05 per cent. of citric acid. On December 18th this sample was of a very light green color and preservation appears to have been perfect. It now shows no further change.

No. 6.—Proportions of the U. S. P. formula with the addition of 0.1 per cent. of citric acid. On December 18th this sample had retained its original pale green color, and at this time preservation appears to have been perfect.

Conclusions.—If syrup of iron iodide is carefully made and with the proper amount of sugar, no preservative whatever is needed. However, to overcome the careless manipulation on the part of some druggists, it has been deemed advisable to add a preservative. Hypophosphorous acid has the advantage of a reducing value which is not possessed by the organic acid suggested for this purpose. It has, however, the disadvantage that in the strength directed it will act upon sugar in strong solutions and darken the syrup. This could be overcome by substituting glycerin for a portion of the sugar directed in the formula.

PETROLATUM LIQUIDUM, U. S. P. VIII (PARAFFINUM LIQUIDUM), WHITE MINERAL OIL.

By S. L. HILTON.

The U. S. P. VIII provides that this substance shall conform to the following description:

A mixture of hydrocarbons, chiefly of the methane series, obtained by distilling off most of the higher and more volatile portions from petroleum and purifying the liquid residue.

A colorless, or very slightly yellowish, oily, transparent liquid without odor or taste, but giving off, when heated, a faint odor of petroleum.

Sp. gr. .870 to .940 at 25° C. Tests as to solubility, acid impurities, fixed oils or fats, either animal or vegetable, and readily carbonizable impurities.

It is proposed for the U. S. P. IX to change the official title to Paraffinum Liquidum. This seems to be wise and in conformity to modern standards. The description, allowing a very slight yellow color, is a mistake, as there is no difficulty in obtaining a colorless oil except the oils of this kind that are produced in this country. The new requirement which requires that it shall be free from fluorescence is proper and not unnecessarily exacting.

From a careful study of a number of samples of white mineral oil, obtained from various sources, the appended table shows that the official requirements can be met without much difficulty; it is further demonstrated that an oil that is usually above the sp. gr. .870 will show more or less paraffin when subjected to a temperature of -4° C., yet in the table two samples, each of the sp. gr. of .875, remained perfectly clear after being subjected to this temperature for eight hours. It is therefore evident that in the process of purification chilling was not thorough or carried on for a sufficient length of time, and the final filtration was not performed at the same temperature. The desire to have as heavy oil as possible for internal administration, as recommended by Dr. Lane, of London, is no doubt accountable for such a large number of samples with a specific gravity lower than .875 becoming opaque or milky at this temperature.

With proper manipulation and care an oil of the sp. gr. .875 should show no separation of paraffin on chilling. Some standard covering this point should be provided; that is, a minimum specific

gravity that will show no separation of paraffin when the oil is subjected to a temperature of at least 0° C.

None of the samples showed an admixture of fixed oils or fats, either animal or vegetable. The test is one that must be carefully applied, or an accident will follow. The neutralizing of the alkali with strong sulphuric acid, after digestion, is violent unless it is added very slowly.

The results of the sulphuric acid test are most interesting, showing almost every shade of brown, and in several cases the only layer became opaque and colored and not conforming to the requirements of the pharmacopœia or the standard as given in the British or German Pharmacopœias.

As to the internal administration of paraffin oil, a number of specialists of this city have used it for several years. The principal method followed by them is to administer from 15 to 50 Cc. at bedtime; in obstinate cases of constipation 15 Cc. administered about one hour before meals, so as to avoid interfering with the process of digestion. With these methods of administration good results have been produced. There are, however, many cases where complaints have been made that the oil will pass out of the intestinal tract involuntarily, very much to the discomfort of the patient, even when given in very small doses. This trouble seems to be more frequent with the administration of one of the popular brands of the market which shows a specific gravity of less than .860. To a certain extent this may account for the growing demand for heavier paraffin oils.

Paraffin oils of a specific gravity of .880 or more are rather more difficult of administration than those of .870 to .875; they adhere to the mouth very closely, and to some are disagreeable and suggestive of castor oil.

An oil aromatized or flavored with some essential oil or combination of oils seems to be growing in demand. I submit ten samples, all of which, no doubt, to some would be agreeable. Personally, peppermint seems to be the most pleasant and agreeable; cardamon a close second. No doubt, many would prefer spearmint, owing to the chewing-gum craze.

The flavoring of paraffin oils must be done with care. From 5 to 25 drops of an essential oil, according to which is used, will be found sufficient for 500 Cc. While this small amount may not give a predominant odor, it must be remembered that the dose administered,

EXAMINATION OF WHITE MINERAL OILS.

Brand.	Price gal.	Color and taste.	Odor.	Sp. gr. 23° C.	Saponif. test.	H ₂ SO ₄ test.	Freezing test, -4° C.
Amalie Gloria, Grade "A".....	\$0.85	Colorless and tasteless	None	.87893	Nil	V. P. B.	Slightly opaque
Amalie Gloria, Grade "B".....	.75	Colorless and tasteless	None	.87732	Nil	V. P. B.	Slightly opaque
Amalie Gloria, Grade "C".....	.65	Colorless and tasteless	None	.85884	Nil	V. P. B.	Clear
Amalie Russian, Grade "A".....	.53	Colorless and tasteless	None	.85953	Nil	Brown	Clear
Amalie Russian, Grade "B".....	.50	Slight fluorescence, slight petroleum taste	None	.85992	Nil	Brown	Clear
Liquid Albolene.....	.40 pt.	Colorless and tasteless	None	.85970	Nil	Brown, oil layer colored	Clear
Zinkseisen, Russian.....	.90	Colorless and tasteless	None	.87688	Nil	V. P. B.	Quite milky
National Aniline Co., No. 2.....	.80	Colorless and tasteless	None	.87546	Nil	Brown	Clear
National Aniline Co., a213.....	.80	Colorless and tasteless	None	.88134	Nil	Brown	Slightly opaque
S. K. & F. Co., Russian.....	—	Colorless and tasteless	None	.87599	Nil	Pale brown	Clear
"Squibbs".....	.40 pt.	Colorless and tasteless	None	.87519	Nil	Pale brown	Slightly opaque
"Olo".....	.34 pt.	Yellow cinnamon	Slight cinnamon	.87076	Nil	Brown, oil layer brown	Slightly opaque
Teralbolia.....	—	Fluorescent and tasteless	None	.85535	Nil	Red brown, oil layer dark brown and opaque	Slightly opaque
Freeman's Russian Mineral Oil.....	.50 pt.	Colorless and tasteless	None	.88257	Nil	Pale brown	Quite milky, ropy separation in layer at top.
Petrolax.....	—	Colorless and tasteless	None	.88165	Nil	Dark brown	Clear
Unknown No. 1.....	—	Slight fluorescence	None	.86812	Nil	Pale brown, oil layer slightly colored	Slightly opaque
Unknown No. 2.....	—	Colorless and tasteless	None	.87765	Nil	Red brown, oil layer dark brown, opaque	Quite milky
White Liquid Vaseline.....	—	Very decided fluorescence	None	.85360	Nil	Pale brown	Quite milky
Barrett & Co., Russian.....	1.00	Colorless and tasteless	None	.8840	Nil		Quite milky
Wilson's Sons White Mineral Oil.....	.70	Sample dirty. Very yellow in color, no examination.					

ABBREVIATIONS AND EXPLANATORY TERMS.

V. P. B. Very pale brown.
Prices stated above are wholesale.
Amalie brands, from L. Sonneborn Sons, Inc., New York.
"Olo," American Olo Company, Llanerch, Pa.
Teralbolia, Robert C. Cadmus, Philadelphia, Pa.
Freeman's Russian Mineral Oil, Aseptic Chemical Company, Chicago, Ill.
Barrett & Co., Importers, Chicago.
Zinkseisen, National Aniline and Chemical Company, E. R. Squibb & Sons, New York.
S. K. & F. Co., Smith, Kline & French Co., Philadelphia, Pa.

15 to 60 Cc., will be sufficient to give a fairly pronounced taste. The samples submitted contain in each 500 Cc. the following amounts of essential oils: Almond, 15 drops; cloves, 10 drops; anethol, 10 drops; cinnamon, 5 drops; peppermint, 15 drops; spearmint, 15 drops; sweet birch, 25 drops; wintergreen, 25 drops; and aromatic, using the oils constituting spirit aromaticus comp., 15 drops.

Another interesting phase of the examination is the various prices charged for these paraffin oils, those with fancy coined names commanding very much more than other oils on the open market, and all, or nearly all, coming from the same source and possibly the same importer. As has been pointed out by Mr. Wilbert, the better or fine grades come from Russia, hence the name Russian Mineral Oil; the American oil usually has a fluorescence, slightly yellow in color, and a more pronounced petroleum odor when heated. The best grades of Russian oil can be purchased for about 80 cents a gallon, while those with trade or coined names will cost from 40 to 60 cents a pint.

The pharmacist should be, and is, able to supply physicians and his patients with an oil of high quality, reasonable in price, and should avail himself of the present opportunity. An oil of at least the sp. gr. .8750 that is colorless, tasteless, and free from fluorescence, that will not show more than a pale brown color with the sulphuric acid test, free from admixture with animal or vegetable oils, and remains clear when subjected to a temperature of 0° C. for four hours, seems to be the oil most desired and, if demanded, can readily be obtained.

THE PHYSIOLOGICAL CHARACTERISTICS OF ACETYLENE, WITH RESPECT TO ITS USE IN MINING.*

By E. E. SMITH, Ph.D., M.D.

Like every other step in the progress of civilization, the use of acetylene involves certain readjustments of previous notions. In the art of illumination, these problems of adjustment have been particularly definite and impelling. Thus, the pine knot did not give way to the candle, probably, without anxious consideration of the danger of spattering, soot making, and extinction by drafts. Many

* A paper read at a meeting of the International Acetylene Association, late in 1913, for a report of which the *Quarterly* is indebted to Secretary A. C. Morrison, 42d St., Building, New York. Reprinted from the *School of Mines Quarterly*, vol. xxxv., 1914, pp. 143-153.

years of careful study were needed to solve the last of the dangers involved in the use of kerosene, while the difficulties connected with illuminating gas and electricity are still with us. This paper will be limited to the problems of adjustment presented by the use of acetylene as an illuminant.

This leads us at once to the inquiry, Is acetylene a direct poison? The answer is no. This question is asked with some seriousness, however, because, on the one hand, of the notoriously toxic action of common illuminating gas, due to the carbon monoxide which enters so largely into its composition, by reason of which the mind of the inquirer is already not only prepared to believe that acetylene is poisonous, but, in fact, in some instances has that idea rigidly implanted there. It is further asked with seriousness, because, in the literature of the subject, we find some views that it is poisonous. Early writers declared that it combined with the blood and had a marked poisonous effect, like carbon monoxide.

Any gas, when it replaces air, if incapable of supporting respiration, is injurious and even fatal, not because it is poisonous but because it deprives the body of oxygen. Because of this, acetylene is capable of doing injury. If it accumulates in some small, unventilated space, like the cabin of a boat, it is entirely capable of shutting off the supply of air, of preventing respiration and hence causing harm and even death. It suffocates because it is incapable of supplying oxygen, without which man cannot live.

When acting in this way, acetylene is not a direct poison; it does not do anything to the body to injure it. It does harm only indirectly, by withholding air. The recognition, then, of injury by suffocation throws no light on our inquiry whether it is a direct poison. The presence of common illuminating gas in air, even to the amount of a fraction of a per cent., is distinctly injurious and may even be fatal, though such air contain an abundance of oxygen. The carbon monoxide contained in illuminating gas enters the blood through the lungs and attaches itself strongly to the coloring matter of the blood, rendering it incapable of taking up the oxygen of air though the air contain oxygen in ample amount. Thus death supervenes not because the body is denied oxygen but because, through the fixation of the coloring matter of the blood, it has lost its capacity to use oxygen. Has acetylene this or any other directly poisonous action? Some early observers said it had. They found fixation of hæmoglobin quite similar to that of carbon monoxide

and accordingly declared acetylene a poison. Moreover, it seemed to exercise the action of a direct poison on animals.

This was ascertained before acetylene was regularly produced from carbide. The acetylene of that date was made by the incomplete combustion of coal-gas, whence more or less carbon monoxide was present in the acetylene obtained, thus accounting for some degree of toxic action of the acetylene examined. Carbon monoxide is the poison of common illuminating gas.

With the discovery of carbide and its use for the production of acetylene, all of this has been changed. It is now found that acetylene from carbide does not contain carbon monoxide, that it does not have the property of fixing hæmoglobin, and that it does not rob the blood of its capacity to take up oxygen from the air and carry it into the tissues. Hence the old allegation that acetylene is a poison because it deprives the blood of its oxygen-carrying capacity is no longer justified.

Another poisonous product sometimes present in the acetylene made by the old combustion process was hydrocyanic acid. Never in large quantities, it yet is so toxic that we can fully appreciate its effect. It is not present in the carbide acetylene and so may be dismissed from consideration. Another charge that is no longer justified is that acetylene is a poison because of the presence of phosphine as an impurity. This forms when carbide is made from limestone containing phosphate, which is reduced by the action of the coke. The selection of limestone free from phosphate has practically obviated this impurity and any poisonous effect of the acetylene consequent thereto. Indeed, the present day product may be said to avoid the pitfalls of impurities so that its effect is determined by the characteristics of acetylene itself. We may consider then whether acetylene, as such, is or is not a direct poison.

My present observations have been directed to the inquiry whether it produced noticeable effect on human subjects when present in increasing amounts up to $2\frac{1}{2}$ per cent. during a period of $2\frac{1}{2}$ hours. To this end, four men, including myself, were enclosed in a room of about 800 cu. ft. capacity; at the beginning and four times subsequently at intervals of a half-hour, acetylene was liberated in the room by throwing 450 grams of carbide into an open tub of water, this corresponding to the liberation of 4 cu. ft. of acetylene each time; that is, 20 cu. ft. in all, $2\frac{1}{2}$ per cent. of the capacity of the room.

To eliminate, as far as possible, the mental effect of the environment, the subjects were engaged in playing a game of cards. They were interrupted only long enough to take readings of their blood pressures, at half-hour intervals. The results of the experiment were quite negative. The game was continued throughout the period, excepting as noted. The blood pressure remained constant with one subject and was very slightly lowered from the inactivity with two, and absolutely no effect was noted that could be ascribed to any poisonous or other action of the acetylene. It was without effect.

This same result has been obtained in experiments on animals. In such amounts as used in the above experiments there is no effect. Indeed, acetylene may be increased up to 20 per cent. and, if the mixture is so made as not to reduce the amount of oxygen, animals may be left in the atmosphere for some time, an hour or more, and will only become drowsy, from which they quickly recover when removed into ordinary air.

With very large quantities, or with 20 per cent. admixtures acting for a longer time, the degree of drowsiness is increased. That is to say, the effect of acetylene in large doses is that of a narcotic, producing loss of consciousness in proportion to its degree of action. When this action is pushed to a fatal termination, the final effect is upon the breathing centre, inhibiting its action and so producing death.

It thus appears that carbide acetylene is not poisonous in the sense that common illuminating gas is, and that in large quantities, acting for some time, it produces a narcotic action. In respect to its toxicity, it presents no problem of adjustment under ordinary conditions. It, of course, may not replace in large degree the atmosphere we breathe, but otherwise no poisonous action need be anticipated.

A number of interesting problems are presented in connection with the use of the acetylene lamp as an illuminant in mines. I do not refer to those conditions where explosive gases are present, where protection from explosions is obtained through the use of the Davy lamp in some of its modifications, but to that large number of mines which are regularly illuminated by the naked flame. For this purpose, the miner's oil lamp has been used for many years. It is light in weight, but its illuminating capacity is strikingly low and, moreover, is obtained at the expense of a smoking-out process that is amazing. It is a tribute to the miner's endurance that in the

past he has accomplished so much under the conditions of poor illumination and soot-laden atmosphere which the use of the oil lamp has meant. The use of the miner's acetylene lamp affords an illumination that is wonderfully efficient and entirely soot-free. Its use raises some questions that we may answer at this time. Before considering these, let us look at some of the problems which the miner has to face, upon which the choice of an illuminant may have some bearing. Of first importance is the composition of the air which he breathes.

For our present purpose we may regard the atmospheric air as a mixture of 21 parts of oxygen and 79 parts of inert gas, mostly nitrogen. It is the oxygen that supports life. The proportion of oxygen may be diminished to a certain extent without noticeable effect, especially if the difference is made up by inert nitrogen. Under these conditions a reduction to 14 per cent. produces little or no physiological effect. When the reduction reaches 12 per cent., there is apt to be slightly deeper breathing, while 10 per cent. is an amount distinctly below what is physiologically advisable. Seven per cent. may be regarded as the fatal point. It is an amount too small to support the life of animal or man for any considerable time. It must be kept in mind that these figures, 10 per cent. the physiological insufficiency and 7 per cent. the fatal point, are for oxygen with inert nitrogen, and without the admixture of poisonous gases.

There is always present in atmospheric air a small amount of carbon dioxide gas, commonly known as carbonic acid. This amount is very small, ordinarily not over 5 parts in 10,000. It is a product of the combustion of organic matter and is present in air exhaled from the body in breathing. As we shall see later, it is also a constituent of mine gases and so is of particular interest to us. I will call attention to what happens when it is added to the air.

To answer this question I have myself made direct observations. The apparatus employed was a closed cabinet, the inside measurements of which were approximately 67 x 30 x 69 in., having a capacity of 80 cu. ft. It was provided with a sliding door. Into the top a pipe entered and connected with three "sprays," one in each third of the top. Through this system gases were introduced. There was a small sample tube, easily movable, so that gas was withdrawn from any position desired within the cabinet, which was connected outside with (a) an exhaust bottle for withdrawing residual air

from the tube; and (b) a gas-sampling tube. Collections were made over mercury and analysis was made over mercury in a Hempel apparatus. The cabinet was tightly built, but not sufficiently so to prevent escape of air sufficient to equalize the pressure without and within the cabinet when gas was introduced. A movable electric fan within the cabinet was adapted to produce motion of the air.

When carbon dioxide was mixed with atmospheric air, it was noted that such mixture produced an increased rate of respiration, even when the proportion of carbon dioxide was small. Rabbits and guinea-pigs showed a marked increase when as much as 4 to 5 per cent. of carbon dioxide was present. With increasing proportions respirations became deep and labored, frequently, as was observed in guinea-pigs, reaching a condition of diaphragmatic spasm. Loss of muscular power developed so that, with guinea-pigs, ability to support the body was lost when the carbon dioxide reached 20 to 25 per cent. These symptoms developed irrespective of whether lamps were burnt in the same atmosphere. With rabbits, when lamps were burning, loss of muscular power appeared with the same proportion of carbon dioxide as with guinea-pigs, but in a single observation made without lamps, the loss of power appeared when the carbon dioxide had reached 36 per cent. No effort was made to determine the percentage of carbon dioxide that would produce death, as it was believed that the proportion producing loss of muscular power represented the limit of possible tolerance. It may be noted, however, that in the experiment carried to 36 per cent. carbon dioxide, the rabbit quickly recovered, two guinea-pigs recovered somewhat slowly, and one guinea-pig died, when the animals were removed into fresh air. Thus it appears that even with guinea-pigs, the fatal carbon dioxide proportion is not much if any below 36 per cent., while the carbon dioxide warning point is not above 4 to 5 per cent.

To test the effect of carbon dioxide on man, 10½ cu. ft. of carbon dioxide were passed into the cabinet, when a young man entered, the door being opened for that purpose and quickly closed. After entering, the fan was started. The rate of respiration at once rose from 18 to 48, being deeper and labored. He almost immediately complained of feeling dizzy. At the end of 2½ min. there was a feeling of impending loss of consciousness. A sample of the air mixture was at once taken and at the end of 3 min. the man came out. His respiration quickly returned to normal, but his face was flushed and he complained for several hours of a slight frontal

headache. Analysis of the sample showed 7 per cent. of carbon dioxide. The experiment indicated that with man the warning point is reached below 7 per cent. of carbon dioxide.

Such experiments lead to the following general conclusions regarding the physiological effects of increasing proportions of carbon dioxide. There is increase in the rate of breathing which, with 3 per cent. dioxide, has become so marked that it gives unquestioned warning to the subject that some unusual condition of the air is rendering it unsuited for breathing. We may call this the physiological warning point for carbon dioxide. When the concentration reaches 8 to 10 per cent., the breathing is not only rapid but has become very labored, a condition termed dyspnea. Beyond 15 per cent., further concentration, instead of increasing respirations, decreases them and the animal becomes narcotized, quite as though a substance like chloroform had been administered. At a concentration beyond 35 per cent. the narcosis becomes fatal.

I have gone into the influence of oxygen decrease and of carbon dioxide increase on breathing and on life because these are conditions that may be presented by the air in mines. Moreover, the oil lamp has been relied upon to indicate to the miner whether or not the mine air is fit to breathe, air that sustains the flame being regarded as safe and air that extinguishes the flame as unsafe to breathe.

The disadvantages of the oil lamp are all too apparent. Its dingy light limits the working capacity of the miner, due to poor illumination. Aside from working capacity, the miner is not so well able to see the elements of danger presented by weakness in overhanging strata or structures. An even greater disadvantage is the production of soot by the flame. This both adds to the personal discomfort, already great, and also to the danger of dust explosions by addition of the soot to the dust-laden atmosphere. These conditions render an illuminant that is brilliant and soot-free a very great advantage. The acetylene lamp supplies such an illuminant in an admirable manner. In connection with its use it is desirable to determine its relation to composition of mine air, so that the miner may know in what way and to what extent it replaces the oil lamp as an index of safety. That is to say, we have here a problem of adjustment to which it is important to give a correct and definite answer.

First, then, let us consider the variations in composition that may be presented by mine air. Because of the limitations of access of outside air and especially because of the formation of gases in

mines, mine air may present a considerable departure from the composition of outside air.

All ordinary foreign gases were known to the early miners as "damps," from the German *damf*, meaning vapor, the specific designation being indicated by an individual prefix. Thus, the gas characterized by its tendency to extinguish the flame was called black-damp, or, since it tends to produce suffocation, choke-damp; the damp producing increased brilliancy of light, white-damp; that with a marked stink, stink-damp; that which readily took fire, fire-damp; the gas resulting from burning or explosion, after-damp, etc. These names were applied long before the composition of the respective gases was known. In consequence of the indefinite basis of the classification, an individual name was in many instances applied to mixtures that presented wide variation in composition.

Black-damp, on chemical analysis, has ordinarily proved to be a mixture of carbon dioxide and nitrogen, the proportion of carbon dioxide varying from very little up to 15 per cent. or perhaps exceptionally 20 per cent. As it is always mixed with more or less air, a corresponding amount of oxygen is present. Other gases, such as methane (fire-damp), carbon monoxide (white-damp), hydrogen-sulphide (stink-damp), also water vapor, may be present in greater or less amount.

We may well ask, then, what the name black-damp indicates. Does it mean carbon dioxide, which is the characteristic constituent; does it mean the carbon dioxide-nitrogen mixture; is it the carbon dioxide-nitrogen-air mixture; or is it the combination of any of these with other gases that are present in the mine air? Unfortunately, there has been no unanimity of usage in regard to this term, it having been used by different writers in almost every one of the above possible meanings.

If we were to establish anew the definition of the term, it would be doubtless wise to adopt a scientific meaning. As the matter stands, our meaning should be decided by priority, which is that black-damp is not simply carbon dioxide but rather a mixture of that with nitrogen in varying proportions, but we must not forget the different usages of individual authors.

Our problem is: How does the admixture of black-damp modify the respirability of mine air and how is this indicated by the oil and acetylene flames? It requires no facts other than those now before us to appreciate that it affects respirability in two ways. It dimin-

ishes the proportion of oxygen which, if reduced to 10 per cent., would be unphysiological and to 7 per cent., fatal; and it increases carbon dioxide which, when present to the amount of 3 to 4 per cent., would produce marked increase in the rate of breathing.

As to when the change in composition, especially the carbon dioxide increase, is indicated by the particular flames, has been the subject of personal experimental observations. The cabinet employed in the experiment previously described was used. In the earlier experiments with carbon dioxide, this gas was fed into the cabinet without previous admixture with air; in the later ones both air and carbon dioxide were fed into the cabinet through meters, entering the cabinet through a common tube. Thus they were well mixed and the rate of flow of each was regulated. Early experiments indicated that various factors influenced the extinction point, both for the oil and acetylene lamp. Let me relate what these factors were and how they exercised their influence.

A. Acetylene Gas Pressure.—From the outset it was observed that the pressure under which the acetylene gas was fed through the burner exercised a marked influence upon the extinction point. That is to say, with a series of lamps in which the acetylene gas pressure varied, as indicated by the character of the flame, it was not difficult, in a mixture of increasing proportion of carbon dioxide, to foretell the order in which the lamps would be extinguished, the lamps with higher acetylene pressure going out first. Indeed, it was frequently observed, where the escape of gas from the burner was under such slight pressure as not to give direction to the flame, that the extinction point would be very much higher than was observed with the ordinary burning flame. Care was therefore exercised to make our observations on lamps in which the gas production showed a normal amount of pressure.

B. Air Movement.—When there was no movement of air, excepting such as resulted from the convection currents produced by the lamps and by the introduction of the gas mixture, the extinction points were: for the acetylene lamps, 23 to 25 per cent. carbon dioxide; for the oil lamps, 12 to 14 per cent. carbon dioxide. With the production of a gentle movement of the air by fanning against the side of the cabinet, the extinction points were appreciably affected, being lowered in the case of the acetylene lamps to 22 to 17 per cent. carbon dioxide; in the case of oil lamps to 12 to 10 per cent. carbon dioxide.

With the production of a strong movement of the air, by direct fanning of the lamps, in two experiments the acetylene lamps were extinguished when the air contained 9.4 per cent. and 9.9 per cent. carbon dioxide, respectively, while the oil lamps were extinguished by the same breeze in atmospheric air.

The movement of the lamps worn on the heads of the miners would produce, in quiet air, the effects that result from a breeze with the lamps stationary. We may conclude, therefore, that in the case of the acetylene lamp the extinction point is lower than 25 per cent., in proportion to the rapidity of motion; and with the oil lamps, correspondingly lower than 14 per cent.

C. Oxygen Proportion.—In the experiments mentioned, the oxygen was reduced only moderately by the admixture of the carbon dioxide in the form of pure gas. Undoubtedly, such reduction tends to lower the carbon dioxide extinction point. The effect, however, is only moderate, since the oxygen in all experiments was distinctly more than would sustain the flame if the specific effect of the carbon dioxide were neglected.

When the admixture of carbon dioxide is in the form of black-damp, however, the question of the oxygen proportion becomes an important factor for consideration. In these preliminary investigations, we were not able to study the effect of black-damp, since with the use of so large a cabinet, the quantity of nitrogen required would be much greater than it was practical to obtain.

D. Humidity.—In a number of experiments, water vapor was introduced into the gas mixture by blowing over the surface of water within the cabinet. In this way, the humidity was raised from approximately 35 to 65 or 80. Any effect upon flame extinction by carbon dioxide that may have resulted was within the limits of variation from the other factors considered. The conclusion is therefore reached that humidity affects the proportion of carbon dioxide required to produce flame extinction only within relatively narrow limits.

Comparing now the effects of carbon dioxide increase on flame extinction and respiration, we note that the first effect is a physiological one, when the proportion reaches 3 to 4 per cent., there being an increase in the respiratory rate that is entirely adequate to warn persons of the atmospheric condition. Flame extinction occurs with oil at 13 per cent. and acetylene at 26 per cent. in still atmosphere, but at 10 per cent. and 17 per cent. with moderate motion. With

either lamp the extinction point is too high above the physiological warning point to make it of value to the miner. The conditions will have been recognized before the extinction point is reached. Should, however, the physiological warning be unheeded, flame extinction will occur, first with the oil and then with the acetylene flame, with either in ample time to prevent loss of life. The margin of safety, though greater with the oil lamp, is adequate with the acetylene.

In considering the influence of oxygen decrease on flame extinction, I shall make use of observations made by Chester S. Heath, under experimental conditions different from those I have described.

He finds that with moderate motion an oil flame is extinguished when the oxygen is reduced to 16.5 per cent.; in still air to 16.2 per cent. With acetylene, at moderate motion, extinction occurred at 12.6 per cent. and was dimmed in still air of the same composition, being extinguished in still air at 11.5 per cent. It thus appears that the oil flame is extinguished with considerably less reduction of oxygen than the acetylene, but that the latter is extinguished before the reduction is fatal to man, which is at 7 per cent. Moreover, in actual mining conditions, where the lamp is worn on the head, there will be sufficient motion; hence extinction will occur at a point somewhere above that observed with the experimental conditions.

Finally, it is not to be forgotten that the condition of extreme oxygen reduction without carbon dioxide increase, which was present in the experimental observations, is not encountered in actual mine air. The specific action of carbon dioxide admixture, that will be found in such conditions, will add its effect to the oxygen decrease and bring about the extinction of an acetylene flame at a point which is still further removed from unphysiological atmospheric conditions, and hence afford an increased margin of safety.

The miner, then, may conclude that a given admixture of black-damp and air in the absence of other foreign gases will support life: (1) if it does not extinguish flame; (2) if it does not produce markedly increased respiration. Any atmosphere which does not give these warnings is respirable, though not necessarily desirable for continuous respiration. It does, however, give warning either physiological, or by the flame of acetylene as well as oil, that is adequate to prevent loss of life.

THE 65TH ANNUAL SESSION OF THE AMERICAN
MEDICAL ASSOCIATION.

By M. I. WILBERT, Washington, D. C.

The 1913 meeting of the American Medical Association was held in Atlantic City, June 22-26, and was attended by 3958 members who took the time and trouble to register. The registration this year is reported to have been considerably larger than that of any of the previous sessions of the Association in Atlantic City. The work of the House of Delegates and its committees and the proceedings of the several sections of the Association are reported at length in the *Journal of the American Medical Association* for July 4, 1914, vol. 63, pp. 73-130. The scientific papers, because of the restrictions imposed by the House of Delegates at the Minneapolis meeting, were fewer in number than in former years, but the subject matter discussed was correspondingly good, the programs for the several sections being generally well carried out.

The Section on Pharmacology and Therapeutics had, as usual, a program containing many papers of pharmaceutical interest. Delegates from the American Pharmaceutical Association were recognized, and Prof. Joseph P. Remington, the chairman of this delegation, in extending the felicitations of the organization he represented, said:

"The American Pharmaceutical Association brings greetings to the American Medical Association. It is meet and proper that two national bodies should exchange greetings, for, however they may differ in function and scope, they are united in principle in the one great object of promoting the health of the nation in combating disease.

"It is gratifying to know that the Pharmacopœia is practically completed, so far as the bulk of the work is concerned. The printing of the Appendix, with the Tables, Reagents, and Volumetric Solutions, will be sent to the printer this week, for this part of the book must be printed first, in order that members may have it for reference in checking up the text of the book.

"During the past year a number of older remedies have been deleted and new remedies admitted. A Committee on Scope which reports upon proposed admissions and deletions have finished their work, but there are still a few questions which can be settled after

the printing is started. One of these questions is the form of so-called bichloride tablets. As is well known, the enormous use of these tablets is a menace to the future growth and prosperity of the nation. The Pharmacopœia cannot check the use of these tablets, but it can at least direct the form for their use which will prevent accident so far as possible through swallowing the tablets or their solution.

"The American Pharmaceutical Association, during the past year, has used its influence in every possible way in controlling or limiting the use of habit-forming drugs by national and State legislation. Committees have been formed from the membership who are working to stamp out this evil.

"The body which I have the honor to represent asks the assistance of your body to aid in framing wise laws which will make it difficult for dopesters to continue their habits, and by limiting the use of these drugs to prescriptions by properly educated physicians, who are earnestly trying to curtail the evil.

"In educational matters Pharmacy has progressed in the direction of raising the standard of education of those entering Pharmacy, and enlarging the curriculum in the colleges. May we not hope that Medicine and Pharmacy will be more closely linked in the future, and that crimination and recrimination will cease, or take the form of constructive criticism, with the intention of remedying the evils and correcting abuses, and will be actuated by harmony between the two professions."

Referring more particularly to the probable scope of the U. S. P. IX, the following table represents the status of that book at the present time:

Number of articles in text of U. S. P. VIII.....	958
U. S. P. VIII articles dismissed from U. S. P. IX list.....	237
Number of articles retained from U. S. P. VIII.....	721
Number of new articles admitted to U. S. P. IX.....	67
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Total number of articles in tentative list of U. S. P. IX.....	788

On motion of Dr. Murray Galt Motter, of Washington, D. C., the Section on Pharmacology and Therapeutics of the American Medical Association adopted the following resolution, which was referred to the House of Delegates, endorsed by that body, and thus officially recognized as the opinion of the American Medical Association:

"WHEREAS, The Pharmacopœia of the United States of America should be, above all, a book designed to protect the public health and prevent the exploitation of the sick and afflicted for profit; now, therefore, be it

"*Resolved*, That the members of the Section on Pharmacology and Therapeutics of the American Medical Association request the House of Delegates to urge upon the Revision Committee to make official in the Pharmacopœia of the United States 'corrosive mercuric chloride pastilles,' so that physicians may not be compelled to prescribe this remedy under a proprietary name. Be it further

"*Resolved*, That this section endorse the form and description of corrosive mercuric chloride pastilles as described in the German Pharmacopœia, namely, of cylindrical shape, twice as long as thick, wrapped individually in paper bearing the name of the medicament, 'corrosive mercuric chloride pastilles,' and the word 'poison' in suitable and striking letters. Be it further

"*Resolved*, That a copy of this resolution be forwarded by the Secretary of the American Medical Association to the President and to each of the officers of the United States Pharmacopœial Convention, and also to the Chairman and to each member of the Committee of Revision of the Pharmacopœia of the United States."

Of the many papers presented in the Section on Pharmacology and Therapeutics, the following contributions were of more immediate interest to pharmacy:

Dr. John F. Anderson, the chairman of the Section on Pharmacology and Therapeutics, in his address discussed some unhealthy tendencies in therapeutics and referred more particularly to the ill-advised use of certain biologic products, such as the Friedmann vaccine for tuberculosis and crotalin in the treatment of epilepsy. In summing up this paper he suggested that, while advances in therapeutics are necessary and clinical trials must be made, these trials should be with adequate controls of otherwise treated cases and under circumstances in which every stage can be watched and the various clinical and laboratory observations be made a matter of unbiased record, and the best interests of the patients thus safeguarded. It is difficult to secure these conditions outside of a well-equipped hospital. Until a new method of treatment has received abundant confirmation of this sort it is unjust—to use no stronger word—to apply it promiscuously to patients who are not under constant observation and are not amenable to instant emergency relief.

In a paper on "The Medical Treatment of Chronic Intestinal Stasis," W. A. Bastedo, of New York, discussed the uses and limitations of many of the aperients and cathartics. In commenting on the now widely used paraffin oil, he called attention to a series of ten samples not one of which complied strictly with the requirements of the Pharmacopœia, and also stated that in writing prescriptions for paraffin oil or liquid petrolatum it is unfortunately true that it is practically necessary to specify some established brand, as the material supplied in retail drug stores very seldom, if ever, complies with the requirements of the Pharmacopœia or is of an otherwise satisfactory nature.

In a paper on active immunization in diphtheria by toxin-antitoxin mixtures, William H. Park, of New York, reported on recent progress in the prophylaxis of diphtheria and reviewed the present-day knowledge regarding immunization and the possible recognition of immunization by skin reaction.

In a paper on the use of diphtheria antitoxin in the treatment of diphtheria, Samuel S. Woody, of Philadelphia, recommended the administration of much larger doses than are used at present, and also asserted that the number of antitoxin units to be administered should be in keeping with the stage of the disease. He also stated that as a prophylactic diphtheria antitoxin was uncertain and in a great measure unsatisfactory in its results, and that to be efficacious in the treatment of diphtheria, antitoxin must be given at the earliest possible moment and in large doses.

In addition to the resolution endorsing the inclusion of pastilles of corrosive mercuric chloride in the Pharmacopœia of the United States, the House of Delegates also adopted the following recommendation of pharmaceutical interest suggested by the Council on Medical Education and endorsed by the reference committee:

"Your committee also recommends that the Council be instructed to urge all medical colleges to adopt the nomenclature of the Pharmacopœia of 1910, and to use the metric system in their teaching."

The scientific exhibit was of unusual interest, and the work displayed was not alone excellent, but much of it was of immediate practical value to the profession. The commercial exhibit attracted considerable attention and was unusually free from objectionable features in the way of proprietary and semi-proprietary preparations not recognized by the Council on Pharmacy and Chemistry.

The officials for the Section on Pharmacology and Therapeutics

for the coming year are: Chairman, R. A. Hatcher; vice-chairman, J. Ray Arneil; secretary, M. I. Wilbert; delegate, John F. Anderson, and alternate, Ray L. Wilbur.

At the opening meeting of the Association on Tuesday morning Dr. Victor C. Vaughan, of Ann Arbor, Mich., was installed as president, and at the concluding session of the House of Delegates on Thursday afternoon Dr. Wm. L. Rodman, of Philadelphia, was selected as the president-elect and San Francisco chosen as the place of meeting for 1915.

BOOK REVIEWS.

DIGEST OF COMMENTS ON THE PHARMACOPEIA OF THE UNITED STATES OF AMERICA AND ON THE NATIONAL FORMULARY FOR THE YEAR ENDING DECEMBER 31, 1912. By M. I. Wilbert and M. G. Motter.

One hardly realizes the vast amount of writing done annually in reference to pharmacopœial matters until one peruses the above useful compilation and the several that preceded it.

We do not say that Charles Rice "built better than he knew," because he knew many things, if all we have learned of him is true, but he certainly built wisely and with the foresight possessed by a great mind when he suggested and carried out the idea of compilation and classification of critical references anent matters pharmaceutical. That we live in a day and under a form of government that sees its way clear to carry this idea to fuller fruition augurs well for pharmacy in this country.

JOHN K. THUM.

ANNUAL REPORT OF THE INVESTIGATIONS CARRIED OUT UNDER THE SUPERVISION OF THE THERAPEUTIC RESEARCH COMMITTEE OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION, VOLUME II, 1913.

This small volume of 111 pages embodies the results of some practical research work that is bound to have an influence for good on medicine and pharmacy. Both physicians and pharmacists would do well to purchase this little volume, which can be obtained for a small sum, for it will put them in possession of some positive knowledge on the possibilities and limitations of some well-known drugs. While it may be true, as is sometimes said, that medicine is not an

"exact science," yet if it is ever to be raised from the slough of empiricism, work of this kind *must* be done and persistently promulgated among the members of the professions.

JOHN K. THUM.

PHILADELPHIA COLLEGE OF PHARMACY.

QUARTERLY MEETING.

The quarterly meeting of the Philadelphia College of Pharmacy was held June 29, 1914, at 4 P.M., in the Library; the President, Howard B. French, in the chair. Fifteen members were present. The minutes of the annual meeting, held March 30, 1914, were read and approved.

The minutes of the Board of Trustees for March, April, and May were read by the Registrar, J. S. Beetem, and approved. The report of the Committee on Necrology was read by the Chairman, and referred for publication in the *AMERICAN JOURNAL OF PHARMACY*.

Professor Stroup reported verbally for the delegates to the Pennsylvania Pharmaceutical Association. The attendance was somewhat smaller than usual. The reception of delegates from other organizations and reports of delegates to other bodies were the features of the first day's session. A large number of papers were, as usual, presented, the one on "Bacterial Vaccines and Serums," by Dr. A. P. Hitchens, being most interesting. The report of the Legislative Committee and the report of the Secretary of the State Pharmaceutical Board were also presented. The president, R. H. Lackey, made a number of recommendations which, after being referred to a special committee, were adopted. The Association elected the former secretary, E. F. Heffner, president, and David J. Reese, secretary. The next meeting is to be held at Forest Park, Pike County.

The delegates to the Delaware Pharmaceutical Association reported verbally by its chairman, Dr. A. W. Miller. The meeting was held at Hotel Du Pont, Wilmington, on June 4th. The reports of the officers and committees occupied the morning session. The meeting was not a very large one, but a very harmonious one. Your delegate was accorded a cordial welcome, who urged upon the members their help to influence congressional action in securing a

site for the statue to Professor Procter in front of the Smithsonian Institution.

The delegates to the New Jersey Pharmaceutical Association reported through the chairman, George M. Beringer. The 44th annual meeting was held at Hotel Breslin, Lake Hopatcong, June 16th to 19th. The absence of other members of the delegation, owing to the commencement exercises of the College occurring at the same time, was very much regretted. The meeting was one of the largest attended and most interesting sessions ever held. The sessions were well attended, and under the able executive the business was thoroughly yet expeditiously considered. Legislative matters were again one of the principal topics considered and the incoming Legislative Committee was instructed to have the proposed new pharmacy law, with a prerequisite clause, again presented to the next Legislature, and to use their best endeavors to have this bill enacted. The Committee on Papers and Queries presented an unusually interesting report. About twenty papers were read and discussed. A number of these were contributions from the members of this College. The subjects covered a wide range: commercial, educational, legal, scientific, and practical pharmaceutical questions were treated in these papers. Of no less interest were the discussions they provoked. The internal affairs and finances of the Association were subjects for earnest consideration. The President, in his annual address, advocated an increase in the dues in order to avoid a deficiency. Mr. John C. Gallagher, of Jersey City, was elected president, and Mr. G. M. Hays Deemer, of Atlantic City, was elected vice-president. The entertainments provided by the Local Committee and Travelling Men's Auxiliary were good and sufficient for the occasion without infracting upon the time needed for business.

Professor Kraemer presented the following resolution referring to a celebration of the fiftieth anniversary of the founding of the Alumni Association:

"As the session of 1914-15 will mark fifty years since the Alumni Association of the Philadelphia College of Pharmacy was established, and as the founders rendered yeoman service in the development of the educational facilities of the College, *Resolved*, That the College recognize this interest in her former students and arrange for a fitting celebration to commemorate this milestone in the history of the Association."

The reading of the paper caused considerable discussion. Mr.

French said that the Alumni Association had been foremost in all the advances the College had made, either as the originator or supporter of these advanced movements. The discussion was further participated in by Messrs. Beringer, Kraemer, Poley, French, Miller, and Stroup, when Mr. Beringer moved that a joint committee of the Board of Trustees and the Alumni Association be appointed to consider the matter. Adopted.

Professor Kraemer presented a framed receipt for two hundred dollars, contributed by the Class of 1889 for the Centenary Fund now in process of collection. On motion, it was voted to place it in the Library.

Professor Kraemer referred to the work which had been done during the past fifteen years, prior to the establishment of the present course in Bacteriology, and requested that a succinct account of the work be compiled from the reports of the Committees on Instruction and Examination.

Mr. Beringer, in commenting on the paper just read, said he wanted to call particular attention to the advances the College has made in its courses of instruction. There should be still further advances made. We should have post-graduate courses. No other college is giving the advanced courses that we are giving, especially in Pharmacognosy. More publicity should be given to the instruction given in the College. Our third-year class should be augmented from graduates of other institutions who are receiving less than we are giving.

The President made the following appointments:

Committee on Nominations: W. A. Rumsey, E. F. Cook, W. L. Cliffe, Otto Kraus, John K. Thum.

Committee on Necrology: Henry Kraemer, Joseph W. England, C. A. Weidemann.

C. A. WEIDEMANN, M.D.,
Recording Secretary.

ABSTRACTS FROM MINUTES OF THE BOARD OF TRUSTEES.

March 3, 1914.—Thirteen members present.

Committee on Property reported that a lunch room had been opened, that the lunches furnished were of good quality, and that

the number of student patrons was greater than had been expected. The caterer expressed his satisfaction at the results of the undertaking, and it was regarded a success. The committee suggested the advisability of larger accommodations for the next session. The committee also reported complaints having been made concerning students smoking throughout the building, and advocated the enforcement of more stringent rules governing this practice, confining smoking to the cemented portions of the first floor and basement.

Committee on Library reported 398 books accessioned during the month, making a total of 6676 books ready for cataloging. Two hundred and forty-one persons had used the Library.

Committee on Examinations presented the results of the recent examinations held at the end of the first semester for the classes of the first, second, and third years.

Committee on By-laws proposed several amendments: To amend Article 8, Section 3. To amend Article 11, making same Article 12, and to introduce a new Article on Scholarships and Fellowships, as Article 11. Action was deferred until the next meeting.

Committee on Athletics presented a communication from the students representing the track team. The committee felt that the matter of athletics was one to be assumed by the Alumni Association and to be under their control and support. The subject was referred to the President of the Alumni Association.

Committee on Membership reported favorably on the application of Miss Agnes Duvoisin; a ballot was taken and she was unanimously elected to active membership.

April 7, 1914.—Thirteen members present. A communication was received from the Recording Secretary of the College, announcing the election of officers for the ensuing year and three Trustees for three years (see this JOURNAL, p. 229).

Nominations for officers of the Board being in order, George M. Beringer was elected chairman; Walter A. Rumsey, vice-chairman, and Jacob S. Beetem, registrar.

The Chairman read a communication from the staff of the "Graduate" 1913, offering to present a loving cup to be awarded to the first-year class 1914, and competed for thereafter under the rules governing the award of the President's Cup. On motion the offer was accepted and the appreciation of the Board expressed.

Dr. A. W. Miller read a communication from Professor Ernest Gilg acknowledging receipt of his Certificate of Honorary Member-

ship, for which he expressed appreciation and offered the College a set of his books. The offer was accepted with the thanks of the Board.

The Chairman announced the Standing Committees for the ensuing year, as follows: Property, Howard B. French, chairman; Library, Samuel P. Sadtler, chairman; Museum and Herbarium, O. W. Osterlund, chairman; Finance, Howard B. French, chairman; Supplies, H. K. Mulford, chairman; Accounts and Audits, C. A. Weidemann, chairman; Instruction, George M. Beringer, chairman; Scholarships, Joseph P. Remington, chairman; Examinations, William L. Cliffe, chairman; Theses, Joseph W. England, chairman; Discipline, Howard B. French, chairman; Announcement, Samuel P. Sadtler, chairman; Commencement, Walter A. Rumsey, chairman; Alumni, Joseph W. England, chairman; Appropriations, composed of chairmen of all committees empowered to make expenditures, also the chairman of the Board of Trustees, the chairman of the Committee on Finance, and the Treasurer.

Mr. French presented souvenirs, consisting of invitations, programs, menus, advertisements, etc., relating to past affairs of the College. These were of historic interest and were referred to the Historical Committee.

Professor Remington referred to the Panama Exhibition in 1915, expressing the thought that it would be to the advantage of the College to exhibit a line of official and N. F. preparations, together with historical matter, and suggested that a committee be appointed to make arrangements and that the College make an early application for space. On motion it was voted that a committee of five be appointed.

April 21, 1914.—Eleven members were present.

Committee on Examinations reported favorably on the application of Prof. Edwin Leigh Newcomb, P.D., for the degree of Master in Pharmacy in course, all the requirements having been complied with. A ballot was ordered and the applicant was unanimously elected to receive the degree at the next commencement.

Committee on Instruction reported that they had held a number of meetings to consider the annual reports from the Faculty. Abstracts from these reports are as follows:

Department of Pharmacy: The record of attendance as now made obligatory has been of special value. The extra lectures on pharmaceutical subjects have been attended by a much larger number of

students than heretofore; the increased time given to this department has permitted considerable additional instruction in Operative Pharmacy. It is thought desirable that this department be furnished with a lantern for illustrating lectures on prescriptions, etc. Numerous slides have been accumulated, and these are used to advantage, but they are not as effective as the projection of the actual prescription.

The course in Commercial Training has been greatly increased, and the former indifference of the students has given way to eagerness to absorb information.

The instructor in Latin reports that his work has been satisfactory.

Department of Chemistry: Professor Sadtler reports upon the work of the second- and third-year classes. By the lengthening of the College year, and the increase in the hours of instruction, a more extended course of instruction is given. In addition to the course of public lectures that have been given in recent years to the third-year classes, it is thought that a series of lectures for the second-year class could be introduced to considerable advantage. As the instruction to the second-year class covers many of the commercial chemicals, it would seem that a series of lectures bearing upon that subject would be especially beneficial.

Department of Materia Medica: Increased attention has been given to the physiological assaying of drugs with good results.

Department of Botany and Pharmacognosy: Advanced methods have been used. With each laboratory lesson a mimeographed outline of the work is given the students, printed on sheets of uniform size to fit in the notebooks used in this department. In the first year the initiative work is on the principal groups of plants, which is a little difficult for the beginner, and interest has been stimulated by periods of debates. A Biological Club has been organized; a program is arranged, and the discussions are illustrated with the lantern. In the second year the subject matter has been presented in groups according to their natural relationships. Two hundred and fifty-four types of drugs have been arranged in twelve-ounce jars, which have been consulted at recess and other times; the reviews have been of great help also. The third-year work has been in the study of chocolate products, spices, and a number of National Formulary drugs. Professor Kraemer, having been relieved of the teaching in Bacteriology, has been enabled to develop a special course in Microscopy

for the Special Chemical students. It is suggested that time be provided for compulsory botanical excursions to be considered as part of the laboratory exercises. The green-house and roof garden continue to be very serviceable in giving instruction.

Department of Analytical Chemistry: The instruction in this department has been carried on in accordance with the published announcement and outlined course. The results have been very satisfactory, and a continuance along the same lines is recommended.

Department of Bacteriology: The attendance at lectures was uniformly good. The laboratory instruction in the regular course will be doubled.

Department of Physical Culture: About two-thirds of the class presented themselves for examination. New record cards have been prepared. Many of the students were found to be under weight and flat-chested, and the proper gymnastic training for these conditions was given.

Physical Director: This report contains a number of interesting items on the work of the department.

May 5, 1914.—Eighteen members present.

Committee on Library reported 472 books shelf-listed, making a total of 7690 books ready to be catalogued. Use of Library for the month by 382 persons.

Committee on Supplies were given power to act in procuring additional microscopes.

Committee on Examinations reported having received a communication from the Secretary of the State Pharmaceutical Examining Board, requesting that the final result of the third-year examinations be recorded in time to comply with the State Board requirements.

President Howard B. French presented to the College, on behalf of Mrs. Mary I. Banks, a check for \$5000 with which to establish a fellowship in memory of her father, the late Clayton French. The following resolution was adopted:

Resolved, That the Board of Trustees of the Philadelphia College of Pharmacy gratefully acknowledge receipt of Five Thousand Dollars through the hands of Mr. Howard B. French from Mrs. Mary I. Banks, to be used in establishing a fellowship in honor of her father, the late Clayton French.

Resolved, That a tablet be erected in the hallway of the College bearing the following inscription:

1824

1890

Clayton French
FELLOWSHIP

Established by his daughter

Mary I. Banks

May 16th, 1914

The Dean moved that the gift be accepted and that the grateful thanks of the College be expressed. It was further resolved that the income from the fund should be used for advanced research work.

Mr. Campbell referred to the N. A. R. D. Convention to be held in August in this city, and favored representation by the College. After discussion, a committee of five, consisting of Messrs. Campbell, Osterlund, Remington, Mulford, and Evans, was appointed to consider the matter and report to the Board.

The Chairman announced the appointment of the Special Committee on Panama Exposition: Joseph P. Remington, chairman; Joseph W. England, Warren H. Poley, H. K. Mulford, C. Stanley French; associates, Professors E. F. Cook, F. X. Moerk, Henry Kraemer. With authority to add to their number.

OSAGE ORANGE, ITS VALUE AS A COMMERCIAL DYESTUFF.

It has long been known in the Southwest that the wood of the Osage orange tree contains a dyestuff that would give a more or less fast yellow color. An examination of the wood from Texas by F. W. Kressmann showed that it not only contains moric acid and morintannic acid, the same as fustic wood, but also that the dyeing principles are present in amount to be commercially valuable. A comparative series of dyeing experiments made with fustic and Osage orange wood and extracts showed the latter to be of equal value with fustic in regard to depth of colors produced, the amount of extract, the character of the dyeing, and fastness to light, weather, washing, etc.—*Science*, vol. xl, July 3, 1914, p. 37.